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Body weight in early and mid-adulthood in relation to subsequent coronary heart disease mortality: 80 years follow-up in the Harvard Alumni Study

Linsay Gray, PhD[a], **I-Min Lee, ScD**[b,c], **Howard D. Sesso, ScD**[b,c], and **G. David Batty, PhD**[a,d,e]

[a]MRC/CSO Social and Public Health Sciences Unit, Glasgow, UK

[b]Harvard School of Public Health, Boston, MA, USA

[c]Brigham and Women's Hospital, and Harvard Medical School, Boston, MA, USA

[d]The George Institute for International Health, University of Sydney, Sydney, Australia

[e]Department of Epidemiology & Public Health, University College London (UCL), London, UK

To the Editor -

In the very few studies conducted,[1-4] obesity in young adults is generally associated with an increased risk of future coronary heart disease (CHD). However, data interpretation is complicated by methodological limitations which include: small study size; a paucity of studies examining the impact of confounding factors; and unexplored mechanisms, including the essentially unknown contributions of early versus later body weight on CHD risk[5-6] which has implications for weight control interventions . In the largest and best characterised study to date we directly address these shortcoming.

Methods

The Harvard Alumni Health Study is a cohort study of men who had a routine medical examination as undergraduates at Harvard University between 1916 and 1950.[7] Measurements of height, weight and blood pressure were made, and students responded to enquiries regarding smoking habits;[7] details on physical activity were ascertained from university records.[6] Questionnaires mailed to surviving alumni in either 1962 or 1966 included questions about height, weight, lifestyle habits, and medical history; a high level of agreement has been shown between these responses and direct measurements.[7] Harvard Alumni Office listings were used to identify decedents and copies of official death

Correspondence to: Dr Linsay Gray, MRC/CSO Social & Public Health Sciences Unit, 4 Lilybank Gardens, Glasgow, UK, G12 8RZ. l.gray@sphsu.mrc.ac.uk.

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certificates were obtained with 99% coverage.[8] CHD deaths were coded according to the Seventh Revision of the International Classification of Disease (ICD 420).

Subjects in the present analyses had complete data on height and weight at both the university medical examination and the following up questionnaire (n=18,995; Table 1). Cox regression was used to model the relation of early and later adulthood BMI with subsequent CHD mortality with sequential adjustment for age, early adult CHD risk factors, mid-life CHD risk factors and mid-life/early adulthood BMI (Table 1). As middle-age BMI is conceivably on the causal pathway of early adulthood BMI and mortality, we also used joint modelling to estimate these inter-relationships.

Results

A maximum of 82.5 years of follow-up (median 56.4 years) gave rise to 2,025 CHD deaths in the 18,995 men. The correlation between BMI in early adulthood and middle age was moderate (r=0.49, p<0.001). Men who were obese in early adulthood had nearly twice the risk of future CHD mortality (hazard ratio=1.83; 95% confidence interval 1.21-2.76) and there was evidence of a linear trend across BMI categories (*ptrend*=0.006) (age-adjusted, Table 1). Adjustment for other confounding variables at college entry, and potential mediating factors in middle age, had little impact. However, when middle-age BMI was added to the multivariable model the predictive capacity of early BMI for later CHD mortality was greatly attenuated (1.21; 0.73-2.02). Early BMI was not significantly related to CHD (p=0.418) in the joint model.

BMI in middle-age was also associated with CHD mortality (*ptrend*<0.001) such that study members who were overweight and obese experienced a 25% and 60% increased risk, respectively (age-adjusted analyses, Table 1). This association persisted following adjustment for all covariates (Models 2 to 5). Similar results were obtained when we categorised BMI according to quartiles, and when total mortality was the outcome of interest.

When we repeated our analyses with multiple imputation (n=19,821), and also when we restricted analysis to the subset of men with no missing data on BMI and potential confounders (n=14,638), the results were essentially unchanged (results not shown). We found similar college BMI–all-cause mortality associations (1.46; 1.16-1.83 for obese) which remained significant after full adjustment (1.38; 1.06-1.81). Stroke mortality was unrelated to college BMI (0.39; 0.05-2.83).

Comment

In this cohort study we found a doubling in CHD mortality risk in men who were obese in early adulthood. This association held after adjustment for both confounding variables in early adulthood and potentially mediating factors in middle-age, but, importantly, was eliminated after taking in account mid-life BMI.

Our findings contrast with the only other study with prospectively measured BMI in both early and later life which found that elevated body weight in adolescence exerted an effect

on CHD after adjusting for adiposity in mid-life.[4] In that study, there were considerably fewer deaths and therefore lower statistical power. In another prospective study, being overweight in college was associated with increased risk of future cardiovascular disease mortality, but no adjustment was made for subsequent BMI.[3]

While the Harvard Alumni Health Study has several advantages – its sample size and number of endpoints, a range of collateral data, and repeated BMI measurements – it is not of course without its shortcomings. While there is growing evidence to suggest that body composition (e.g., central adiposity) in middle- and older-age is associated with CHD, the only measurement of adiposity available to us was BMI. Further, the present analyses are restricted to men; it is plausible, although perhaps unlikely, that different results may have been seen in women.

In conclusion, the apparent doubling of future CHD risk in men who were obese in early adulthood was effectively eliminated following control for BMI in middle-age. These results require replication in other studies.

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References

1. Owen CG, Whincup PH, Orfei L, et al. Is body mass index before middle age related to coronary heart disease risk in later life? Evidence from observational studies. Int J Obes. Aug; 2009 33(8): 866–877.
2. Lawlor DA, Martin RM, Gunnell D, et al. Association of body mass index measured in childhood, adolescence, and young adulthood with risk of ischemic heart disease and stroke: findings from 3 historical cohort studies. Am J Clin Nutr. Apr; 2006 83(4):767–773. [PubMed: 16600926]
3. Jeffreys M, McCarron P, Gunnell D, McEwen J, Davey Smith G. Body mass index in early and mid-adulthood, and subsequent mortality: a historical cohort study. Int J Obes Relat Metab Disord. Nov; 2003 27(11):1391–1397. [PubMed: 14574351]
4. Must A, Jacques PF, Dallal GE, Bajema CJ, Dietz WH. Long-term morbidity and mortality of overweight adolescents. A follow-up of the Harvard Growth Study of 1922 to 1935. N Engl J Med. Nov 5; 1992 327(19):1350–1355. [PubMed: 1406836]
5. Wilsgaard T, Jacobsen BK, Schirmer H, et al. Tracking of cardiovascular risk factors: the Tromso study, 1979-1995. Am J Epidemiol. Sep 1; 2001 154(5):418–426. [PubMed: 11532783]
6. Paffenbarger RS, Wing AL. Chronic disease in former college students. X. The effects of single and multiple characteristics on risk of fatal coronary heart disease. Am J Epidemiol. 1969; 90(6):527–535. [PubMed: 5362860]
7. Paffenbarger RS, Thorne MC, Wing AL. Chronic disease in former college students, VIII: characteristics in youth predisposing to hypertension in later years. American Journal of Epidemiology. 1968; 88:25–32. [PubMed: 12418454]
8. Lee IM, Sesso HD, Paffenbarger RS Jr. Physical activity and coronary heart disease risk in men: does the duration of exercise episodes predict risk? Circulation. Aug 29; 2000 102(9):981–986. [PubMed: 10961961]

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Table 1

Hazard ratios (95% confidence intervals)[a] for the relation of body weight in early adulthood and middle-age with future coronary heart disease (CHD) mortality in the Harvard Alumni Health Study (N=18995)

	Age-adjusted[b]	Age- and early adult CHD risk factor-adjusted[c]	Age- and midlife CHD risk factor-adjusted[d]	Age- and midlife/early adulthood BMIadjusted[e]	Fully-adjusted[f]
Number of men	18995	15408	18019	18995	14638
Deaths from CHD	2025	1580	1797	2025	1401
Early adulthood (18.4 yr)					
Underweight (<18.5 kg/m^2)	1.03 (0.88, 1.22)	1.00 (0.83, 1.21)	1.13 (0.95, 1.33)	1.16 (0.98, 1.37)	1.20 (0.98, 1.46)
Normal weight (18.5 - <25 kg/m^2)	1.00 (ref)	1.00	1.00	1.00	1.00
Overweight(25 - <30 kg/m^2)	1.29 (1.09, 1.51)	1.35 (1.13, 1.62)	1.28 (1.08, 1.52)	1.07 (0.90, 1.27)	1.12 (0.91, 1.37)
Obese (≥30 kg/m^2)	1.83 (1.21, 2.76)	1.84 (1.17, 2.89)	1.77 (1.14, 2.75)	1.35 (0.88, 2.05)	1.21 (0.73, 2.02)
p-value for trend	0.006	0.002	0.07	0.93	0.90
Per one SD (2.52 kg/m^2) increase in BMI	1.09 (1.04, 1.13)	1.10 (1.04, 1.16)	1.09 (1.04, 1.13)	1.01 (0.96, 1.06)	1.01 (0.94, 1.07)
Middle-age (46.1 yr)					
Underweight	0.89 (0.48, 1.65)	0.81 (0.41, 1.64)	1.09 (0.59, 2.04)	0.90 (0.48, 1.68)	1.02 (0.51, 2.06)
Normal weight	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Overweight	1.25 (1.15, 1.37)	1.23 (1.11, 1.37)	1.22 (1.11, 1.34)	1.22 (1.11, 1.34)	1.18 (1.06, 1.33)
Obese	1.60 (1.25, 2.03)	1.72 (1.32, 2.25)	1.49 (1.15, 1.92)	1.49 (1.15, 1.92)	1.54 (1.14, 2.08)
p-value for trend	<0.001	<0.001	<0.001	<0.001	0.001
Per one SD (2.55 kg/m^2) increase in BMI	1.19 (1.14, 1.24)	1.20 (1.15, 1.26)	1.16 (1.11, 1.21)	1.18 (1.13, 1.24)	1.18 (1.12, 1.25)

[a] Hazard ratios obtained from Cox regression

[b] Adjusted for age in early adulthood

[c] Early adult CHD risk factors include cigarette smoking status (never, past, or current), physical activity (<2, 2 to <5, ≥5 hours per week, or varsity athletics) and blood pressure; sample limited to men with complete data on potential confounders

[d] Mid-life CHD risk factors include type 2 diabetes and hypertension sample limited to men with complete data on mediating variables

[e] Contains all covariates in prior models

[f] Results for early adulthood are adjusted for BMI in mid-life, those for mid-life are adjusted for BMI in early adulthood sample limited to men with complete data on potential confounders and mediating variables